ORIGINAL RESEARCH

Stroke Incidence and Survival in American Indians, Blacks, and Whites: The Strong Heart Study and Atherosclerosis Risk in Communities Study

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***Background*—**American Indians (AIs) have high stroke morbidity and mortality. We compared stroke incidence and mortality in AIs, blacks, and whites.

***Methods and Results*—**Pooled data from 2 cardiovascular disease cohort studies included 3182 AIs from the SHS (Strong Heart Study), aged 45 to 74 years at baseline (1988–1990) and 3765 blacks and 10 413 whites from the ARIC (Atherosclerosis Risk in Communities) Study, aged 45 to 64 years at baseline (1987–1989). Stroke surveillance was based on self-report, hospital records, and death certificates. We estimated hazard ratios for incident stroke (ischemic and hemorrhagic combined) through 2008, stratified by sex and birth-year tertile, and relative risk for poststroke mortality. Incident strokes numbered 282 for AIs, 416 for blacks, and 613 for whites. For women and men, stroke incidence among AIs was similar to or lower than blacks and higher than whites. Covariate adjustment resulted in lower hazard ratios for most comparisons, but results for these models were not always statistically significant. After covariate adjustment, AI women and men had higher 30-day poststroke mortality than blacks (relative risk=2.1 [95% CI=1.0, 3.2] and 2.2 [95% CI=1.3, 3.1], respectively), and whites (relative risk=1.6 [95% CI=0.8, 2.5] and 1.7 [95% CI=1.1, 2.4]), and higher 1-year mortality (relative risk range=1.3–1.5 for all comparisons).

***Conclusions*—**Stroke incidence in AIs was lower than for blacks and higher than for whites; differences were larger for blacks and smaller for whites after covariate adjustment. Poststroke mortality was higher in AIs than blacks and whites. **(*J Am Heart Assoc*. 2019;8:e010229. DOI: 10.1161/JAHA.118.010229.)**

Key Words: American Indians • blacks • health disparities • stroke

Stroke is the fifth-most common cause of death in the United States[1] and a leading cause of disability. In 2014, American Indian (AI) and Alaska Native people had higher self-reported prevalence of stroke (5.4%) than blacks (4.5%) or whites (2.5%).[2] AIs and Alaska Natives also have among the highest burdens of many stroke risk factors, most notably hypertension, diabetes mellitus, obesity, and smoking.[3] Stroke mortality for AIs and Alaska Natives has been reported as lower than for other groups,[4] but racial misclassification typically leads to underestimating disease-specific mortality rates in this population.[5] In spite of these statistics, AIs and Alaska Natives are under-represented in public health research on stroke incidence and mortality.[6] In the SHS (Strong Heart Study), the only large, population-based cohort study of cardiovascular disease in AIs,[7] stroke incidence and poststroke mortality from 1988 to 2004 were higher than reported for blacks and whites in other prospective studies,[8] but comparisons in this context are difficult because of different durations of follow-up and different distributions of other risk factors across cohorts.

The ARIC (Atherosclerosis Risk in Communities) Study is a large, mostly biracial, population-based prospective study that recruited participants from 4 sites across the United States.[9]

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Clinical Perspective

What Is New?

- This study pooled data from 2 cohort studies to estimate differences in stroke incidence and poststroke mortality in American Indians compared with blacks and whites.
- Stroke incidence in American Indians was similar to or lower than blacks and higher than whites.
- Thirty-day and 1-year case-fatality was higher in American Indians than both blacks and whites.

What Are the Clinical Implications?

- Our results are consistent with causal models in which rural residence leads to barriers in accessing timely medical care for a stroke event, and in which diabetes mellitus is a major cause of stroke disparities in American Indians compared with whites.

ARIC investigators reported higher stroke incidence in black than white participants,[10] but the cohort did not include AIs. The SHS and ARIC share many similarities in study design and timelines: Baseline exams began in 1988 for the SHS (age range, 45–74 years) and in 1987 for the ARIC (age range, 45–64 years). In this analysis, we pooled SHS and ARIC data to compare stroke incidence and poststroke mortality in AIs versus blacks and whites. Our a priori hypotheses were that AIs in the SHS would have higher stroke incidence and poorer poststroke survival than their black and white counterparts in the ARIC, even after accounting for age, sex, and other stroke risk factors.

Methods

Transparency and Openness

The data used for this analysis are subject to oversight from the Publications and Presentations Committees of the SHS (https://strongheartstudy.org/) and ARIC (https://www2.cscc.unc.edu/aric/). In addition, SHS data are subject to tribal sovereignty agreements that require tribal approval before dissemination of data or results to third parties. Because of these constraints, requests from qualified researchers to access the data used in this analysis must be submitted to the SHS and ARIC. Upon approval from both cohort studies, the data set may be obtained from the corresponding author (Muller).

Human Subjects Protections

Institutional and tribal review boards approved procedures for each cohort study, and participants gave written informed consent. The Institutional Review Boards at the University of Minnesota and Washington State University and publications committees for the SHS and ARIC approved these analyses. We obtained all necessary tribal approvals before submitting the manuscript for publication. Two authors had full access to all the data and take responsibility for data integrity and analysis.

Study Populations

The SHS was launched in 1988, funded by the National Heart, Lung, and Blood Institute to study longitudinal risk factors for cardiovascular disease in AIs.[7] The SHS comprised 13 AI tribes and communities in 3 primarily rural regions: Southwest, Southern Plains, and the Northern Plains. All tribal members aged 45 to 74 years were invited to participate, with a total baseline enrollment of 4549 people. Data collection included detailed personal history and lifestyle questionnaires, a clinical exam, and laboratory measurements with blood samples. The SHS conducted follow-up and morbidity and mortality surveillance to adjudicate cardiovascular disease events and deaths, most recently through December 31, 2008. Of the original 4549 participants, 1033 were removed because 1 community withdrew consent.

The ARIC Study was launched in 1987 and funded by National Heart, Lung, and Blood Institute to investigate atherosclerosis and cardiovascular disease in a cohort of primarily black and white adults who were aged 45 to 64 years at the baseline exam.[9] The ARIC used tailored probability sampling to recruit participants at 4 field sites (Washington County, MD; Forsyth County, NC; Jackson, MS; Minneapolis suburbs, MN), with 15 792 (27% black) participants enrolled at baseline.[11] Race was measured by self-report. Annual telephone interviews were conducted to assess hospitalizations, self-reported events, and overall health status. We used data for adjudicated events and mortality through December 31, 2011.

Stroke Ascertainment

The SHS adjudication protocol for stroke followed diagnostic criteria based on international standards.[7,12] Mortality surveillance was conducted by examination of State Health Department death certificate data; Indian Health Service, autopsy, or coroner's report records; and key informant interviews with physicians or family members. Two physicians reviewed potential events, and adjudication by the full Mortality Committee resolved disagreements. Two neurologists then reviewed potential stroke events for a final diagnosis (not a stroke; possible stroke; or definite stroke). Morbidity surveillance was based on hospital chart abstraction and personal interview of participants. The well-enumerated and relatively

closed tribal populations in the SHS led to mortality and morbidity follow-up rates generally exceeding 99%.[8,13,14]

The ARIC protocol for stroke adjudication was conducted in 2 phases.[10] First, putative stroke-related hospitalizations or deaths were identified in annual telephone contacts with participants or next of kin; by review of local hospital discharge records using *International Classification of Diseases, Ninth Revision* (*ICD-9*) codes (430–438), keywords indicating cerebrovascular disease, or reference to relevant imaging or time spent in a neurovascular intensive care unit; and from death certificates. Second, formal adjudication began with standardized abstraction of hospital and death records by a single trained nurse. Events were then classified by computer algorithm as definite or probable ischemic or

Table 1. Baseline by Age, Study, and Race Among Cohort Participants Who Were Stroke Free at Baseline

	SHS	ARIC	
	American Indian	Black	White
	(n=3182)	(n=3765)	(n=10 413)
Age, y, n (%)			
45 to 54	1558 (49)	2190 (58)	5342 (51)
55 to 64	1038 (33)	1540 (41)	5009 (48)
65 to 74	586 (18)	35 (1)	62 (1)
Female, n (%)	1858 (58)	2309 (61)	5532 (53)
Highest education, n (%)			
0 to 11th grade	1302 (41)	1549 (41)	1722 (17)
High school graduate or bachelor's degree	1764 (55)	1069 (28)	4750 (46)
Postgraduate education	116 (4)	1147 (31)	3941 (39)
Current alcohol consumption, n (%)	1345 (42)	1207 (32)	6814 (65)
Smoking, n (%)			
Current	1209 (38)	1119 (30)	2573 (25)
Former	1042 (33)	913 (24)	3674 (35)
Never	931 (29)	1733 (46)	4166 (40)
Body mass index, mean (SD) kg/m^2	31 (6)	30 (6)	27 (5)
Waist/hip ratio, mean (SD)	0.95 (0.07)	0.92 (0.08)	0.93 (0.08)
Blood lipids, mean (SD) mg/dL			
Low-density lipoproteins	121 (33)	137 (43)	137 (38)
High-density lipoproteins	46 (14)	55 (18)	51 (17)
Congestive heart failure, n (%)	100 (3)	247 (7)	380 (4)
Coronary heart disease, n (%)	108 (3)	142 (4)	516 (5)
Systolic blood pressure, mean (SD) mm Hg	127 (19)	129 (21)	118 (17)
Diastolic blood pressure, mean (SD) mm Hg	77 (10)	80 (12)	72 (10)
Hypertension, n (%)			
None	982 (31)	785 (21)	4698 (45)
Borderline	1028 (32)	825 (22)	2417 (23)
Hypertensive	1172 (37)	2155 (57)	3298 (32)
Fasting glucose, mean (SD) mg/dL	148 (74)	117 (55)	104 (28)
Diabetes mellitus, n (%)			
None	1505 (47)	2600 (69)	8427 (81)
Impaired fasting glucose	533 (17)	485 (13)	1175 (11)
Diabetic	1144 (36)	680 (18)	811 (8)

ARIC indicates Atherosclerosis Risk in Communities Study; SHS, Strong Heart Study.

Table 2. Blood Pressure Measured at the Baseline Exam and Antihypertensive Medication Among Hypertensive Cohort Members (Top), and Fasting Glucose Among Diabetic Cohort Members (Bottom)

	American Indian	Black	White
People with hypertension*	(n=1172)	(n=2155)	(n=3298)
Blood pressure at exam			
Systolic, mean mm Hg (SD)	142 (20)	137 (23)	130 (20)
Diastolic, mean mm Hg (SD)	82 (11)	84 (13)	76 (11)
Medication and control†			
No medication, n (%)	464 (40)	535 (25)	723 (22)
Medicated, poor control, n (%)	308 (26)	603 (28)	560 (17)
Medicated, good control, n (%)	400 (34)	1017 (47)	2015 (61)
People with diabetes mellitus‡	(n=1144)	(n=680)	(n=811)
Fasting glucose at exam, mean mg/dL (SD)	207 (75)	200 (87)	172 (66)
Fasting glucose ≤125 mg/dL, n (%)	31 (3)	71 (10)	90 (11)

*Results presented only for people with prevalent hypertension at their baseline exam,
†Medication=antihypertensive drugs; good control=blood pressure <140/90 mm Hg at baseline exam; poor control=blood pressure ≥140/90 at baseline exam.
‡Results presented only for people with prevalent diabetes mellitus at their baseline exam.

hemorrhagic stroke, possible cryptogenic stroke, out-of-hospital fatal stroke, or nonstroke using National Stroke Survey criteria.[15] Data were also reviewed and classified by an ARIC neurologist or physician, and disagreement with the classification was resolved by a second independent physician reviewer.

Measures

We used a combined indicator of ischemic and hemorrhagic stroke as our outcome. There were not enough hemorrhagic events for separate analyses by type; the proportions of hemorrhagic strokes were similar in the 2 cohorts.[8,10] For each person who experienced incident stroke, we calculated age at onset and binary indicators of 30-day and 1-year poststroke survival. Demographic variables included race (AI tribal members from the SHS; black and white participants from the ARIC), baseline age, sex, and years of education categorized as: 0 to 11 years=did not graduate high school, 12 to 16 years=high school graduate through bachelor's degree, and 17 years=postgraduate education. Birth-year tertile was categorized by birth years of 1920 to 1930, 1931 to 1938, and 1939 to 1947, based on tertiles for the pooled data set. The primary outcome was any incident definite stroke observed by age 90 (oldest attained age in the ARIC). We considered stroke risk factors that were assessed similarly in both studies or could be standardized post hoc to minimize study-specific differences. Alcohol consumption and smoking were self-reported and classified as current, former, or never; we used a binary indicator of current alcohol consumption in this analysis.[16–18] Body mass index and blood lipids (low-density lipoprotein, high-density lipoprotein) were measured during study exams. Hypertension status was defined as borderline (systolic blood pressure=120–139 or diastolic blood pressure 80–89 mm Hg measured at the study visit) or prevalent (systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or using antihypertensive medication). We defined good control as blood pressure ≤140/90 mm Hg measured at the baseline exam. For the pooled analysis, we defined glucose metabolism as impaired (fasting glucose=110–125 mg/dL measured at the study visit) or prevalent diabetes mellitus (fasting glucose ≥126 mg/dL, documented diabetes mellitus diagnosis, or use of antihyperglycemic medication). We did not include SHS diabetes mellitus cases defined only by the 2-hour oral glucose challenge or ARIC cases defined only by nonfasting blood glucose samples, because each was not available in the other cohort. We defined good control as fasting glucose ≤125 mg/dL at the baseline exam. Both cohorts assessed prevalent stroke and other cardiovascular disease (coronary heart disease and myocardial infarction, congestive heart failure) by self-report at the baseline exam.

Statistical Analysis

We excluded ARIC participants with race other than black or white (48), participants with prevalent stroke in the SHS (28) or ARIC (286), and ARIC participants with unknown baseline stroke status (362). We then excluded participants with any missing data on covariates (306 AIs, 399 blacks, and 519 whites), and SHS participants born before 1920 (183) to align

with birth years in ARIC. Sensitivity analyses, using multiple imputation for missing values, resulted in negligible differences to point estimates and CIs; we report results for the complete case analysis.

All inferential analyses were conducted separately for women and men. We estimated primary stroke incidence as rates per 100 000 person-years for AI, black, and white racial groups by attained age and birth cohort. We used Cox regression to compare stroke hazards by race with attained age as the time scale, so that each participant entered the model at his or her baseline age. Nonstroke deaths were treated as censored observations. We fit 3 separate Cox models: (1) unadjusted; (2) adjusting for residual confounding by birth year; and (3) additionally adjusting for lifestyle and health factors measured at baseline and included in the pooled data set. Study site was collinear with race for all SHS and most ARIC locations and so was not included as a covariate. We tested for effect measure modification between race and birth year. Analyses were stratified if effect-measure modification was present. Results are presented as point estimates with 95% CIs. We tested the proportional hazards assumption for all models based on a threshold of P=0.05 and conducted stratified analyses to accommodate violations of this assumption.

For people who experienced stroke during follow-up, we used logistic regression to estimate racial differences in 30-day and 1-year poststroke mortality. Models were estimated as described for incident stroke, except that we included age at stroke event as a covariate. We used marginal standardization to report risk differences and risk ratios for AIs compared to blacks and whites.[19,20] We used Stata software (version 14.1; StataCorp LP, College Station, TX) for all analyses.[21]

Results

After exclusions, 17 360 SHS and ARIC participants were included in the analysis (Table 1). Lower percentages of AIs had postsecondary education than blacks and whites, and higher percentages were current smokers. AIs and whites had lower prevalence of hypertension than blacks, but AIs had the highest prevalence of borderline hypertension and prevalent diabetes mellitus. Among people with hypertension, AIs had higher mean systolic blood pressure than both blacks and whites (Table 2). Hypertensive AIs were also less likely than their black and white counterparts to be medicated and in good control at the baseline study exam. Among people with diabetes mellitus, AIs had higher mean fasting glucose and lower percentages of people with fasting glucose in good control. Cumulative stroke risk in AIs (women, 146/1858=7.9%; men, 96/1324=7.3%) was lower than in blacks (women, 243/2309=10.5%; men, 173/1456=11.9%) and higher than whites (women, 280/5532=5.1%; men, 333/4881=6.8%). As shown in Table 3, higher proportions of AIs and blacks with incident stroke experienced the event before age 70. AIs who experienced incident stroke had a much higher risk of death within 30 days of the event than both blacks and whites. These disparities persisted, although with smaller magnitude, for deaths within 1 year of the stroke.

In general, AIs had lower stroke incidence than blacks and higher stroke rates than whites for rates stratified by attained age category and birth cohort (Table 4). In Cox regression analyses, we found evidence of effect-measure modification between race and birth year (P=0.001). Therefore, we

Table 3. Stroke Events, Age at Event, and PostStroke Mortality for Women and Men in the Strong Heart Study (American Indian) and Atherosclerosis Risk in Communities Study (Black, White)

	American Indian	Black	White
Women			
Total stroke events	146	243	280
Age at stroke event, y	N (%)	N (%)	N (%)
45 to 49	1 (1)	1 (<1)	3 (1)
50 to 54	6 (4)	14 (6)	7 (3)
55 to 59	16 (11)	29 (12)	17 (6)
60 to 64	22 (15)	46 (19)	33 (12)
65 to 69	29 (20)	63 (26)	50 (18)
70 to 74	31 (21)	40 (17)	70 (25)
75 to 79	24 (17)	34 (14)	63 (23)
80 to 90	17 (12)	16 (7)	37 (13)
Poststroke mortality			
30 days	29 (20)	25 (10)	39 (14)
1 year	44 (30)	51 (21)	67 (24)
Men			
Total stroke events	96	173	333
Age at stroke event, y	N (%)	N (%)	N (%)
45 to 49	1 (<1)	6 (4)	1 (<1)
50 to 54	8 (8)	10 (6)	7 (2)
55 to 59	7 (7)	25 (15)	22 (7)
60 to 64	23 (24)	37 (21)	50 (15)
65 to 69	22 (23)	46 (27)	79 (24)
70 to 74	14 (15)	25 (15)	83 (25)
75 to 79	14 (15)	16 (9)	56 (17)
80 to 90	7 (7)	8 (5)	35 (11)
Poststroke mortality			
30 days	18 (19)	14 (8)	32 (10)
1 year	28 (29)	39 (23)	63 (19)

Table 4. Stroke Incidence Rates Per 100 000 Person-Years for Women and Men in the Strong Heart Study (American Indian) and Atherosclerosis Risk in Communities Study (Black, White)

	American Indian		Black		White	
	Person-Years	Rate† (95% CI)	Person-Years	Rate† (95% CI)	Person-Years	Rate† (95% CI)
Women						
Total participants	(n=1858)		(n=2309)		(n=5532)	
Attained age, y*						
45 to 54	4748	147 (70–309)	7111	211 (127–350)	15 030	67 (36–124)
55 to 64	10 596	359 (261–493)	17 284	434 (346–544)	41 379	121 (92–159)
65 to 74	8277	725 (563–934)	15 638	659 (543–799)	42 334	284 (237–339)
75 to 90	3650	1123 (827–1525)	4658	1074 (814–1416)	15 487	646 (531–786)
Birth cohort						
1920 to 1931	8726	825 (655–1040)	11 494	853 (700–1039)	3605	411 (350–482)
1932 to 1938	7706	441 (315–618)	16 166	501 (403–623)	42 731	213 (173–262)
1939 to 1947	11 654	343 (252–468)	18 164	352 (276–450)	38 215	107 (79–146)
Men						
Total participants	(n=1324)		(n=1456)		(n=4882)	
Attained age, y*						
45 to 54	3557	253 (132–486)	4181	383 (235–625)	11 258	71 (36–142)
55 to 64	7025	416 (291–596)	9901	626 (488–803)	34 098	211 (168–266)
65 to 74	5264	683 (493–948)	8752	811 (643–1024)	36 002	450 (386–525)
75 to 90	1762	1192 (777–1828)	2427	989 (663–1476)	12 844	709 (577–870)
Birth cohort						
1920 to 1931	5042	972 (735–1286)	7202	903 (708–1151)	33 093	556 (481–642)
1932 to 1938	4695	575 (394–839)	8743	675 (523–871)	35 471	276 (227–337)
1939 to 1947	8633	232 (150–359)	10 039	488 (369–646)	28 050	182 (138–239)

*Category includes all participants who were in the age range at any time during follow-up.
†Rate per 100 000 person-years.

estimated all Cox models separately by birth-year tertile and verified no residual interactions or violations of the proportional hazards assumption. In unadjusted analyses, AI women in the earliest birth-year cohort had lower stroke rates than black and higher rates than white women (Table 5). Hazard ratios increased from earliest to latest birth cohort for both comparisons; in the most recent birth-year cohort, AI women had nearly equal and not statistically significantly different rates as blacks and over 3 times the rates of whites. Among men, the opposite pattern emerged for AIs compared with blacks, with nearly equal rates in the earliest birth-year cohort and progressively lower hazard ratios with more-recent birth years. AI men in all 3 birth-year cohorts had higher stroke risk than whites in unadjusted models, although estimates were not statistically significant in the latest birth-year cohort.

For most comparisons, the fully adjusted models resulted in greater magnitude of differences for AIs compared with blacks and substantially attenuated differences compared with whites. Most of these effects were not statistically significant. Additional analyses revealed that changes in point estimates for fully adjusted models were almost entirely driven by the higher baseline prevalence of diabetes mellitus in AIs than in blacks and whites, especially notable in the youngest birth-year cohort (Table 6).

In logistic regression models of poststroke mortality, after covariate adjustment AIs had higher risk of 30-day and 1-year mortality compared with blacks, with differences of approximately equal magnitude for both sexes (Table 7). AIs also had higher risks of 30-day and 1-year mortality compared with whites, although these were not statistically significant for women.

Discussion

We found that AIs in the SHS had lower stroke risk than blacks and higher risk than whites in the ARIC before adjusting for lifestyle and health factors. The larger impact of

Table 5. Hazard Ratios From Cox Regression of Incident Stroke by Race and Birth Cohort Tertile

	American Indian vs Black	American Indian vs White
	Hazard Ratio (95% CI)	Hazard Ratio (95% CI)
Women		
Unadjusted		
Birth years 1920 to 1931	0.84 (0.62, 1.14)	1.79 (1.35, 2.38)
Birth years 1932 to 1938	0.91 (0.61, 1.38)	2.24 (1.51, 3.34)
Birth years 1939 to 1947	1.06 (0.71, 1.59)	3.52 (2.26, 5.49)
Adjusted for birth year		
Birth years 1920 to 1931	0.79 (0.56, 1.10)	1.68 (1.22, 2.29)
Birth years 1932 to 1938	0.92 (0.61, 1.38)	2.34 (1.50, 3.34)
Birth years 1939 to 1947	1.16 (0.77, 1.74)	3.87 (2.46, 6.06)
Adjusted for all covariates*		
Birth years 1920 to 1931	0.73 (0.52, 1.04)	1.11 (0.78, 1.58)
Birth years 1932 to 1938	0.75 (0.51, 1.19)	1.12 (0.71, 1.75)
Birth years 1939 to 1947	0.82 (0.52, 1.28)	1.48 (0.89, 2.46)
Men		
Unadjusted		
Birth years 1920 to 1931	0.97 (0.67, 1.41)	1.62 (1.18, 2.22)
Birth years 1932 to 1938	0.82 (0.52, 1.29)	1.64 (1.18, 2.29)
Birth years 1939 to 1947	0.53 (0.32, 0.91)	1.29 (0.89, 1.86)
Adjusted for birth year		
Birth years 1920 to 1931	0.98 (0.67, 1.44)	2.09 (1.36, 3.21)
Birth years 1932 to 1938	0.82 (0.52, 1.29)	2.11 (1.37, 3.25)
Birth years 1939 to 1947	0.54 (0.31, 0.92)	1.14 (0.71, 1.83)
Adjusted for all covariates*		
Birth years 1920 to 1931	0.98 (0.67, 1.47)	1.50 (0.88, 2.54)
Birth years 1932 to 1938	0.68 (0.42, 1.09)	1.50 (0.87, 2.59)
Birth years 1939 to 1947	0.42 (0.24, 0.74)	0.75 (0.42, 1.33)

*Adjusted for birth year, education, alcohol consumption, smoking, body mass index, and prevalent disease (cardiovascular disease, hypertension, or diabetes mellitus).

Table 6. Diabetes Mellitus Prevalence at Baseline for American Indian Participants of the Strong Heart Study Compared With Black and White Participants of the Atherosclerosis Risk in Communities Study, by Birth Cohort

	American Indian vs Black	American Indian vs White
	Prevalence Ratio (95% CI)	Prevalence Ratio (95% CI)
Women		
Birth cohort		
1920 to 1931	1.7 (1.4, 2.0)	4.5 (3.7, 5.2)
1932 to 1938	2.0 (1.7, 2.4)	6.4 (5.2, 7.7)
1939 to 1947	2.4 (1.9, 2.9)	6.6 (5.0, 8.2)
Men		
Birth cohort		
1920 to 1931	1.8 (1.4, 2.2)	3.0 (2.4, 3.5)
1932 to 1938	2.1 (1.6, 2.7)	5.1 (4.0, 6.2)
1939 to 1947	2.3 (1.7, 2.9)	5.0 (3.8, 6. 2)

adjusting for risk factors in younger birth cohorts mirrored the higher diabetes mellitus prevalence in AIs compared with blacks and whites at their baseline study exams, which may reflect the emerging diabetes mellitus epidemic among AIs during the 20th century. Among women, hazard ratios comparing AIs with whites increased from the oldest to youngest birth-year tertiles, congruent with research showing that whites benefitted more than other racial groups from recent declines in stroke morbidity and mortality.[22] Among men, comparisons were relatively consistent across birth-year cohorts for AIs compared with whites, whereas AI men had progressively lower stroke risk than blacks from oldest to youngest birth-year cohort. Possible explanations for these sex-based differences could include differences in prevalence and control of diabetes mellitus or hypertension or changes in other risk factors, such as sedentary lifestyle or smoking, that differed by race and sex. Such hypotheses could be further explored in longitudinal analyses that account for time-varying risk factors across multiple cohort study exams. Another potential explanation is that the less-precise comparisons between AI and black women could have yielded point estimates with opposite trend than observed for men by chance alone.

AIs in the SHS had substantially higher 30-day poststroke mortality than blacks or whites in the ARIC. Differences were less striking for 1-year mortality, although AIs still showed higher risk than blacks or whites. CIs were less precise than in analyses of stroke incidence because of the smaller sample size and smaller number of events, and results were not statistically significant for all strata. However, the direction and magnitude of point estimates were similar in analyses stratified by sex, which lends strength to our interpretation of higher poststroke mortality in AIs.

Declining stroke incidence since the 1960s also coincided with declining mortality, leading to stroke being downgraded from third- to fifth-most common cause of death in the United States.[1] Evidence suggests that non-Hispanic whites benefitted more from these trends than people of other races and ethnicities.[23] In our analysis, mortality in AIs was higher than for blacks and whites at 30 days and 1 year after stroke onset. These disparities could reflect barriers to timely access of acute healthcare services in the primarily rural, reservation

Table 7. Racial Differences in 30-Day and 1-Year Mortality After Primary Stroke

	American Indian vs Black		American Indian vs White	
	RD (95% CI)	RR (95% CI)	RD (95% CI)	RR (95% CI)
Women				
30-day mortality				
Unadjusted	9.6 (2.1, 17.1)	1.9 (1.0, 2.9)	5.9 (−1.7, 13.6)	1.4 (0.8, 2.1)
Adjusted*	11.2 (2.8, 19.7)	2.1 (1.0, 3.2)	8.3 (−0.1, 17.5)	1.6 (0.8, 2.5)
1-year mortality				
Unadjusted	9.1 (0.0, 18.2)	1.4 (0.9, 1.9)	6.2 (−2.7, 15.2)	1.3 (0.9, 1.7)
Adjusted*	10.1 (0.0, 19.6)	1.5 (1.0, 2.0)	6.2 (−4.0, 16.6)	1.3 (0.8, 1.7)
Men				
30-day mortality				
Unadjusted	10.1 (4.3, 15.8)	2.1 (1.3, 2.9)	7.8 (2.2, 13.4)	1.7 (1.1, 2.2)
Adjusted*	11.1 (5.0, 17.2)	2.2 (1.3, 3.1)	8.5 (2.0, 15.0)	1.7 (1.1, 2.4)
1-year mortality				
Unadjusted	8.1 (1.1, 15.1)	1.4 (1.0, 1.7)	8.5 (1.9, 15.2)	1.4 (1.1, 1.8)
Adjusted*	8.7 (1.5, 16.0)	1.4 (1.0, 1.8)	8.3 (0.9, 15.7)	1.4 (1.0, 1.8)

RD indicates risk difference; RR, risk ratio.
*Adjusted for sex, age at stroke event, birth year, education, alcohol consumption, smoking, body mass index, and prevalent disease (cardiovascular disease, hypertension, or diabetes mellitus).

communities of the SHS; greater stroke severity or poorer underlying health status in AIs; disparities in healthcare quality or rehabilitation services; or some combination of these and other explanations. They may also reflect the need to tailor public health interventions and clinical care protocols for specific populations and contexts. In particular, our study design cannot disentangle race from geographical location, given that there was little regional overlap between SHS and ARIC study sites. In addition to rurality, geographical location can correlate with factors, such as diet, insurance coverage, and aspects of the built environment, that might affect stroke risk and outcomes.

The inferential implications of adjusting for risk factors depend on one's view of race as an exposure for disease.[24] We view race as a social and political invention that correlates with biological (eg, ancestry) and social (eg, discrimination) causes of disease.[25] Adjusting for health conditions, such as hypertension and diabetes mellitus, in this context could be interpreted as evaluating the magnitude of disparities that persist after accounting for differences in known risk factors.[26,27] This view also places epidemiological study of racial disparities in a social justice context.[28] However, the validity of these estimates depends, in part, on the absence of uncontrolled confounding between the health condition and outcome. We therefore opted to present results both with and without covariate adjustment. The crude estimates are useful for demonstrating disparities experienced by AIs, whereas risk-factor adjustment may help elucidate targets for intervention to reduce stroke disparities, such as diabetes mellitus prevention or improved access to emergency health care.

It is beyond the scope of this study to make causal inference about race-based stroke disparities or to make clinical recommendations for reducing incidence and mortality among AI people. Our results are consistent with causal models in which rural residence leads to barriers in accessing timely medical care for a stroke event, and in which diabetes mellitus is a major cause of stroke disparities in AIs compared with whites. This interpretation is also supported by recent studies showing that hospital quality improvement programs can decrease racial disparities in stroke outcomes.[29,30] These and other explanations could elucidate high-impact policy, public health, and clinical care targets for stroke prevention. First, however, future studies that more narrowly focus on specific potential causes should be conducted to confirm and extend our findings. In particular, research with stringently standardized methods is needed to verify the startling poststroke case fatality disparities we observed in this pooled analysis.

This analysis has several limitations. First, because all SHS participants were AI and all ARIC participants were black or white, we cannot disentangle racial comparisons from other study-specific factors. We attempted to minimize this concern by pooling SHS data with ARIC, a cohort with similar design and timing, and by setting attained age as the scale for Cox

regression models rather than time elapsed since the baseline exam. Nevertheless, study-specific differences in stroke ascertainment cannot be ruled out as a partial explanation for our findings. Second, it is unclear to what extent our results can generalize to the larger populations of AIs, blacks, and whites across the United States. Nearly all of the black participants in the ARIC resided in the so-called stroke belt of the United States,[31] which could contribute to the higher incidence of stroke compared with AIs in this analysis. Third, the inferential analysis relies on untestable assumptions of no uncontrolled confounding; correct specification of the Cox and logistic regression models; and consistency of exposure, meaning that any given race label confers the same health effects on everyone to whom it is applied.[32] This assumption is unlikely to be met, given that the meaning of race and its impact on health likely vary across culture, geography, and time. Therefore, our results must be interpreted as reflecting overall associations while acknowledging the likelihood that population-level differences may not apply equally to all individuals. Fourth, for some comparisons, we lacked a robust sample size and effect estimates were relatively imprecise.

Conclusion

AIs in the SHS had lower stroke risk than blacks and higher risk than whites in the ARIC. After adjusting for risk factors, differences were strengthened for comparisons with blacks and attenuated for comparisons with whites. This phenomenon was strongest in the youngest birth-year tertile. AIs who experienced stroke had substantially higher risk of 30-day poststroke mortality than both blacks and whites, with higher risks of smaller magnitude for 1-year poststroke mortality. Our analysis suggests that the diabetes mellitus epidemic in AIs may be a strong factor in high stroke rates among SHS participants and also highlights profound disparities in poststroke survival, especially in the first month after onset. Further epidemiological and experimental studies are needed to verify this finding, and to understand and intervene on the causes for earlier poststroke death risk in AIs.

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Disclosures

None.

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